

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

TALECRIS BIOTHERAPEUTICS, INC. and)	
BAYER HEALTHCARE LLC,)	
)	
Plaintiffs,)	
)	C. A. No. 05-349-GMS
v.)	
)	JURY TRIAL DEMANDED
BAXTER INTERNATIONAL INC. and)	
BAXTER HEALTHCARE CORPORATION,)	PUBLIC VERSION
)	
Defendants.)	
)	
)	
)	
)	
BAXTER HEALTHCARE CORPORATION,)	
)	
Counterclaimant,)	
)	
v.)	
)	
TALECRIS BIOTHERAPEUTICS, INC. and)	
BAYER HEALTHCARE LLC,)	
)	
Counterdefendants.)	

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

OF COUNSEL:

James G. Gilliland, Jr.
Susan M. Spaeth
Anne M. Rogaski
TOWNSEND and TOWNSEND and
CREW LLP
379 Lytton Avenue
Palo Alto, CA 94301
(650) 326-2400

Philip A. Rovner (#3215)
POTTER ANDERSON & CORROON LLP
Hercules Plaza
P.O. Box 951
Wilmington, DE 19899-0951
(302) 984-6000
E-mail: provner@potteranderson.com

*Attorneys for Defendant Baxter International
Inc. and Defendant/Counterclaimant
Baxter Healthcare Corporation*

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I. Introduction

The asserted patent in this case, U.S. Patent No. 6,686,191 (“the ‘191 patent”), was obtained by precariously navigating prior art covering each separate aspect of the alleged invention. To obtain these claims, the applicant focused on a purported “surprising” cause and effect and, in view of that cause and effect, obtained patent claims covering a particular sequence of two process steps, both of which were acknowledged by the applicant as previously known. Generally, the asserted claims in this case relate to treatment of antibody solutions with a trialkylphosphate (“TNBP,” solvent) and a detergent (commonly known in the art as a “solvent/detergent treatment”) to inactivate viruses, which the applicant asserts causes a surprisingly and unexpectedly higher and undesirable “anticomplement activity” (or “ACA”), followed immediately by subjecting the antibody solution to a previously known incubation process to lower the alleged unexpectedly higher, and undesirable, ACA. The precise order and proximity of these steps is critical to these claims, as the applicant admitted that it was already known in the art to treat antibody solutions with solvent/detergent and to incubate antibody solutions under the conditions used in the ‘191 patent. It was the purported “surprising” effect – increased ACA caused by solvent/detergent treatment, followed by incubation to reduce that increased ACA to a level acceptable for intravenous administration – that persuaded the U.S. Patent and Trademark Office (“Patent Office”) to issue the ‘191 patent claims.

The asserted claims of the ‘191 patent contain numerous terms that defy definition because they are so indefinite. Other claim terms are capable of being construed, but must be limited to the particular conditions disclosed in the ‘191 patent because other conditions would not lead to the “surprising” effect that was the basis for the alleged invention. To construe most of these terms, the Court need go no further than the claims

themselves, the '191 patent specification and the prosecution history of the '191 patent. For a few claim terms, however, it is useful to review the positions the applicant has taken in other venues and parallel experiments the named inventor performed (but which results he did not disclose to the Patent Office), all of which help define the proper boundaries of the claims. When all of this evidence is considered, Defendants Baxter Healthcare Corporation and Baxter International Inc. (collectively, "Baxter") submit, the proposed constructions set forth herein should be adopted.

II. Brief Technical Background¹

A. The '191 Patent

United States application serial number 08/532,211 ("U.S. application"), which ultimately led to issuance of the patent-in-suit, the '191 patent, was filed with the Patent Office on or about September 22, 1995. The '191 patent issued about eight and a half years later on or about February 3, 2004. The named inventor on the '191 patent is William R. Alonso. On information and belief, the '191 patent was assigned to Bayer Healthcare LLC.

The '191 patent contains 24 claims, three of which (Claims 1, 21 and 23) are independent process or product-by-process claims. Plaintiffs have asserted the following claims in this action: Claims 1, 2, 7-12, 15-20, 23 and 24. The claim terms in dispute are found in Claims 1 and 2. Claim 2 depends from Claim 1, which provides:

¹ A Glossary of Terms and various technical references are attached to the Declaration of Anne M. Rogaski in Support of Defendant Baxter International Inc. and Defendant/Counterclaimant Baxter Healthcare Corporation's Claim Construction Brief ("Rogaski Decl.") filed herewith, to provide the Court with background technical information, but are unnecessary to determine the proper construction of the disputed claim terms.

1. A method of treating a solution of antibodies which may have virus activity, the method comprising

a) contacting the solution with a trialkylphosphate and a detergent under conditions sufficient to substantially reduce any virus activity and resulting in an increased level of anticomplement activity; and

b) then incubating the solution of step a) under conditions of controlled time, pH, temperature, and ionic strength, such that the increased anticomplement activity of the solution is reduced to an acceptable level suitable for intravenous administration. Rogaski Decl., Ex. 2, Claim 1.

Claim 2 adds the requirement that the ACA is reduced to “less than about 60 CH₅₀ units/mL.”

Generally, the asserted claims pertain to methods of treating a solution of antibodies that may have virus activity by first treating the solution with a solvent and a detergent to inactivate viruses, which step purportedly increases the level of ACA in the solution, and then “incubating” the solvent/detergent treated solution under particular conditions to lower the ACA. The claims recite this incubation decreases the increased level of ACA of the antibody solution to levels suitable for intravenous administration.

B. Intravenous Immunoglobulins

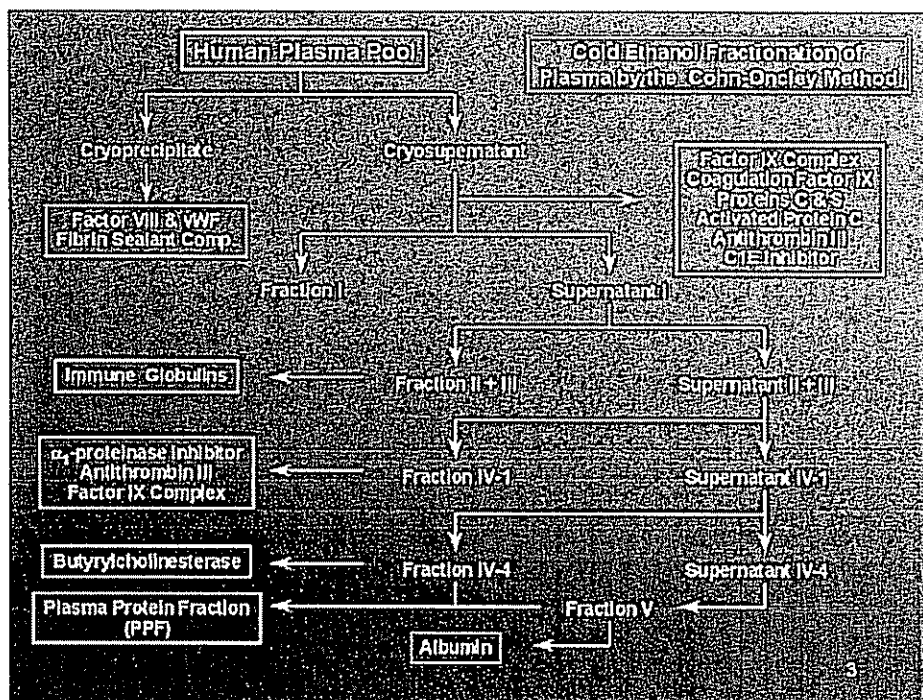
Individuals suffering from a variety of conditions, including Kawasaki Syndrome, Chronic Lymphocytic Leukemia and Idiopathic Thrombocytopenic Purpura, lack sufficient antibodies (also called “immune globulins” or “immunoglobulins”) to adequately fight off infections. Administering antibodies to these individuals can improve their resistance to infection. A variety of companies, including Baxter Healthcare Corporation (“BHC,” one of the Defendants herein), manufacture purified plasma therapeutic solutions containing relatively high concentrations of antibodies that help patients with immune deficiency conditions fight off infection. Indeed, a liquid

immunoglobulin product, “Octagam” was produced by Octapharma at least by early 1995. *See*, Rogaski Decl., Ex. 17.

C. Fractionation, Purification And Virus Reduction Processes

1. Cohn-Oncley Fractionation

Antibodies are fractionated and purified from human plasma obtained from blood pooled together from a large number of blood donors. Because the plasma comes from human donors, it may include viruses or other impurities that are preferably eliminated in the process of purifying the antibody solutions. As a first step, the collected plasma is separated from other blood constituents and then is processed (or “fractionated”) to obtain different plasma components that can be used to treat different diseases. The fractionation of different plasma components is carried out through a well-known process known as the “Cohn-Oncley method” (named after the people who developed the process), and modifications thereto. A simplified illustration of the fractionation products of the Cohn-Oncley method is shown in the figure below.



(<http://worldaidsday.nih.gov/dait/lynch/slide3.htm>)

The Cohn-Oncley method has many different possible pathways that can be chosen to isolate a given plasma component. These pathways involve precipitating different plasma components using different conditions. The “Fraction II+III” pathway from the Cohn-Oncley method can be used to isolate antibodies (referred to as “Immune Globulins” in the above figure). While the primary purpose of the Cohn-Oncley method is to fractionate different plasma components, the method is also known to remove at least some viruses that may have originated from the blood. *See, e.g.,* Rogaski Decl., Ex. 3, p. 323. For example, when “Supernatant I” in the figure above is separated into Fraction II+III and “Supernatant II+III,” any viruses that remain with Supernatant II+III are thus removed from Fraction II+III, and so will not be present in the solution containing Immune Globulins.

Different types of antibodies can then be purified from Fraction II+III. For

example, antibodies known as IgA, IgG and IgM are present in Fraction II+III. *See*, Rogaski Decl., Ex. 4, Col. 12:1-6; Col. 5:60-6:16.

The fractionation steps between pooled plasma and the (*e.g.*) Fraction II + III intermediate are often called “upstream” fractionation or processing steps. The purification steps between the (*e.g.*) Fraction II + III intermediate and the purified immunoglobulin product are often called “downstream” purification or processing steps.

2. Solvent/Detergent Treatment

It is important to ensure that as few as possible viruses are present in an antibody preparation prior to administration to a patient. To maximize the viral safety of purified antibodies, multiple steps can be utilized to remove or inactivate viruses.

In the early 1980s, the New York Blood Center (“NYBC”) invented a solvent/detergent virus inactivation process for inactivation of hepatitis B, non-B, non-A, and HIV viruses in plasma or associated with various plasma proteins. *See* Rogaski Decl., Ex. 5, p. 8. A patent for this invention issued in 1985. Rogaski Decl., Ex. 6. As the ‘191 patent acknowledges, the NYBC solvent/detergent process “gained acceptance as being efficacious in the inactivation of lipid-enveloped viruses” Rogaski Decl., Ex. 2, Col. 1:44-53 and Ex. 5, Section I, pp. 1-6. Solvent/detergent treatment was found to inactivate lipid-enveloped viruses, such as HIV and hepatitis, by disrupting the lipid membrane that envelopes the virus, thus destroying the protective layer of the virus and inactivating the virus. *See, e.g.*, Rogaski Decl., Ex. 8, p. 521. To the extent any lipid-enveloped viruses remain after the Cohn-Oncley method is carried out, solvent/detergent²

² The “solvent” in the solvent/detergent treatment is typically trialkyl-N-butyl phosphate (“TNBP”), which is a trialkylphosphate. The “detergent” in the solvent/detergent treatment can be selected from several reagents, including “sodium cholate” (“cholate”),

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treatment can be used to reduce such viruses.

3. Low pH Incubation

Another way to inactivate viruses is by holding an antibody solution at a particular temperature (usually from about 21°C to about 37°C, depending on the time the solution is held) and pH (usually around pH 4.0-4.4) for a sufficient length of time to inactivate the viruses. These low pH incubations have been known to inactivate viruses since at least as early as 1986. *See, e.g.*, Rogaski Decl., Ex. 9, p. 394. Indeed, the '191 patent itself refers to prior art processes of "incubation of [immunoglobulins] under controlled conditions of time, temperature and pH." Rogaski Decl., Ex. 2, Col. 1:64-2:5 and Col. 11, References 9 and 10 (Rogaski Decl. Exs. 10 and 11). Moreover, low pH incubations have been used to reduce anticomplement activity since as early as 1962. *See* Rogaski Decl., Ex. 12, p. 164.

Importantly, low pH incubations have been used together with a solvent/detergent treatment step by many scientists since at least as early as 1988 (including Prince (NYBC, 1988), Ng (Miles, 1993, which eventually became Bayer and then Talecris), Tsay (Miles, 1993, which eventually became Bayer and then Talecris), Eriksson (Pharmacia, 1994), Gehringer (Octapharma, published 02/03/1993) and Octapharma. *See* Rogaski Decl., Ex. 13, p. 6944; Ex. 14, p. 82; Ex. 4, Cols. 5-6; Ex. 15; Ex. 16, Col. 3 (in European Patent), 2 (in U.S. Counterpart); and Ex. 17, p. 7.

Footnote continued from previous page

"Tween-80" (also referred to as "Tween" or "polysorbate"), and "Triton X-100." *See, e.g.*, Rogaski Decl., Ex. 5, Section I, p. 2; Ex. 6.

4. Other Purification/Virus Reduction Steps

In addition to the steps set forth above, manufacturers often employ other downstream processing steps that further purify particular types of antibodies (*e.g.*, IgGs or IgMs) or further inactivate or remove viruses, to the extent any remain after other processing steps. For example, some companies, like BHC, employ steps such as chromatography columns to further purify the protein of interest and nanofiltration to further remove viruses to the extent any remain by that stage of the process.

Chromatography columns can be designed in different ways. Some chromatography columns bind to the proteins of interest, allowing other substances in the solution to flow through the column and be removed; other chromatography columns bind to contaminant proteins and allow the proteins of interest to flow through the column. However designed, chromatography columns are important purification steps. In addition, chromatography columns called “anion exchange columns” can lower ACA. *See, e.g.*, Rogaski Decl., Ex. 18, Col 2 and Ex. 19, pp. 112-114

Nanofiltration steps have been used to remove viruses, to the extent any remain after prior virus inactivation or removal steps. Nanofiltration physically prevents larger molecules (such as large viruses) from passing through a filter, while allowing the antibody solution to pass through, thereby removing larger viruses from the antibody solution.

D. Anticomplement Activity

In addition to striving to make antibody solutions purified and virus-free, antibody solutions are also subject to certain release criteria or parameters.³ One of these release

³ Some of these release criteria are set by, and all are approved by, the pertinent

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criteria for IgG intravenous (“IGIV”) products is an upper limit of “anticomplement activity” (“ACA”).⁴ ACA relates to how an immune globulin solution will interact with the complement system. The human immune system has many complex subsystems, one of which is the complement system. *E.g.*, Rogaski Decl., Ex. 20. The complement system is a series of enzymatic cascades activated by antibody-antigen complexes. Activation of the complement cascade results in a series of reactions that amplify an immune response to a pathogen and can result in lysis of bacteria and initiation of an inflammatory response.

A purified antibody solution can contain some antibodies that are altered or aggregated such that the antibodies activate complement *in the absence of* an antibody-antigen complex. Very generally, the ACA of the solution is a measure (by a particular ACA assay) of the ability of a solution to bind complement proteins (and thereby initiate these enzymatic cascades) in the absence of an antigen. If an antibody solution has a high ACA and is administered intravenously, anaphylactic shock and death can result.

Unlike pH or temperature, ACA cannot be measured directly. Instead, ACA is determined indirectly through a biological assay. One measure of ACA involves a very complicated type of assay that measures the amount of protein in a solution that is capable of “activating” 50% of the complement protein in an optimally titrated

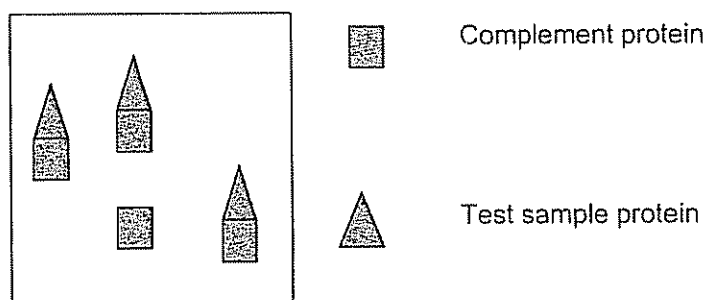
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regulatory agency(ies) before a licensed product may be sold.

⁴ In the United States, there is no specific FDA-mandated release criteria for ACA. Each company validates its own ACA assay and establishes the criteria for its own immunoglobulin product. In Europe, the ACA release criteria for immunoglobulins is set forth in the European Pharmacopoeia.

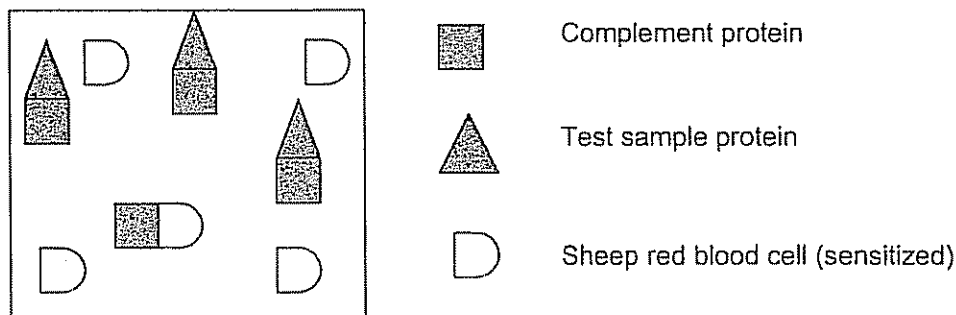
complement and red blood cell/hemolysin system. Several different assays for determining this measure of ACA were known prior to 1995.

A simplified illustration showing the general principle of an ACA assay is shown below, for illustration purposes only. A generic ACA assay measures the amount of complement proteins consumed (or “activated”) by the antibody solution. The assay first incubates a sample from an antibody solution (*i.e.*, that ultimately would be administered to a patient) with a predetermined amount of complement protein (usually from the serum of a guinea pig). If the antibody test sample contains any protein that can activate complement (the “test sample protein”), it will bind to the complement, thereby taking up or consuming a certain amount of complement (*e.g.*, making the consumed complement unavailable to react with antibody-antigen complexes). In the illustration below, three test sample proteins bind to three of the four complement proteins.



Next, the test sample/complement mixture is combined with a solution containing sheep red blood cells (“SRBCs”) sensitized with “hemolysin.” If there is any complement remaining (*i.e.*, if it has not been completely consumed by the anticomplement activity of the test sample protein), such remaining complement will lyse (or burst) the sensitized SRBCs. In the illustration below, the only available complement protein lyses one of the SRBCs. The amount of lysis caused by the only available

complement is measured.



Since the amount of complement originally added to the test sample is known (in this simplified example, four complement proteins), the ACA of the test sample protein can be determined by subtracting the amount of complement that caused lysis of the SRBCs (one) from the original predetermined amount of complement (four). In this simplified example, the test sample protein contains three ACA units.

The above-described general ACA assay principle measures ACA in “CH₅₀” units.⁵ However, there is no single ACA assay. Rather, ACA assays are developed and validated for particular IGIV products. Some assays are based upon the discussion of complement fixation (a related but different assay than an ACA assay) in a book edited by Kabat and Meyer. Rogaski Decl., Ex. 21. More recently, and at least by 1995, the European Pharmacopoeia (which sets standards for pharmaceuticals sold in Europe) has published an assay protocol for measuring ACA.

Although most, if not all,⁶ ACA assays are based upon the general principles set forth above, each assay likely follows a different particular protocol or uses different

⁵ Generally, a CH₅₀ unit is the amount of complement that results in lysis of 50% of the optimally sensitized SRBCs.

amounts or types of the necessary reagents, *e g* , test solution, complement, hemolysin and/or SRBCs. Rogaski Decl. Ex. 19, Abstract. Using complement, hemolysin and SRBCs from different vendors or sources may yield different ACA results. Moreover, ACA results may be different depending on the operator performing the assay or other variables. Indeed, it has been noted in the art that variability in the assay can even result from using red blood cells from different sheep. *See*, Rogaski Decl. Ex. 21, p. 149 and Ex. 22, p. 107. Accordingly, companies must specifically evaluate and determine the variability and precision associated with their ACA assays. The variability depends on the particular assay, but can be 10-20%, or even higher. Because of this, determining ACA levels with any degree of precision is difficult. The variability inherent in ACA assays also makes comparison of ACA results from a single ACA assay difficult. To further complicate evaluation of ACA levels, ACA results from different ACA assays (even those used by a single company) cannot be correlated with each other. *See*, Rogaski Decl. , Ex. 28, pp. 83:12-84:24 and Ex. 23, pp. 148-149

Ultimately, through the purification, virus inactivation/removal and ACA assays described above, viruses in IGIV solutions can be inactivated or removed and ACA levels measured to ensure that the solutions can be safely administered intravenously.

III. Legal Standards for Claim Construction

A. The Role of Claim Construction In A Patent Infringement Suit

Patent infringement analysis entails two steps. The first step is to determine the meaning and scope of the patent claims asserted to be infringed, and the second step involves comparing the properly construed claims to the accused infringing device. *Markman v. Westview Instruments, Inc* , 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). Claim construction is determined as a matter of law. *Id.* at

372 (1996) (“[T]he construction of a patent, including terms of art within its claim, is exclusively within the province of the court.”).

B. Claim Construction Methodology

Last year, the Federal Circuit confirmed the methodology that should be undertaken to properly construe claim terms. *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*). This methodology places primary emphasis on the intrinsic record, including the claims, the specification, and the prosecution history, and relegates extrinsic evidence to secondary status in most cases.

1. Claim Terms Are Given Their Ordinary and Customary Meaning To One of Ordinary Skill in the Art At the Time of Invention

Claim construction begins with an inquiry into how a person of ordinary skill in the art would understand the claim term at the time of invention, *i.e.*, the effective filing date of the application. *Phillips*, 415 F.3d at 1313, *citing Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004). This inquiry is “based on the well-settled understanding that inventors are typically persons skilled in the field of the invention and that patents are addressed to and intended to be read by others of skill in the pertinent art.” *Id.* As the Court explained in *Multiform*:

It is the person of ordinary skill in the field of the invention through whose eyes the claims are construed. Such person is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning and usage in the field. The inventor’s words that are used to describe the invention -- the inventor’s lexicography -- must be understood and interpreted by the court as they would be understood and interpreted by a person in that field of technology. Thus the court starts the decision-making process by reviewing the same resources as would that person, *viz.*, the patent specification and the prosecution history.

Multiform Desiccants, Inc. v. Medzam, Inc., 133 F.3d 1473, 1477 (Fed. Cir. 1998).

Claim construction requires analysis of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent to a layperson, the court must examine “the claims themselves, . . . the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art” to determine what a person of skill in the art would have understood the term to mean. *Phillips*, 415 F.3d at 1314, *quoting Innova*, 381 F.3d at 1116.

2. The Claims Are of Primary Importance In Claim Construction

The Federal Circuit in *Phillips* reaffirmed that the claims themselves are of primary importance in claim construction. *Phillips*, 415 F.3d at 1314, *citing Vitronics Corporation v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) (“[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms.”). Accordingly, the court should look at the context in which a claim term is used in the claim to determine its proper meaning. *Id.* Other claims of the patent, both asserted and unasserted, also can shed light on the meaning of a claim term. *Phillips*, 415 F.3d at 1314, *citing Vitronics*, 90 F.3d at 1582 (“Because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims.”).

Differences among claims also can be helpful in understanding the meaning of particular claim terms. *Phillips*, 415 F.3d at 1314. Where different terms are used in different claims, it is presumed that the inventor meant something different in those different claim terms. *Nystrom v. Trex Co., Inc.*, 424 F.3d 1136, 1143 (Fed.Cir. 2006), (“When different words or phrases are used in separate claims, a difference in meaning is presumed”).

3. The Specification Is the Single Best Guide to Claim Construction

The *Phillips* Court also reaffirmed the paramount importance of the specification in claim construction. For purposes of claim construction, the claims “do not stand alone,” but rather are part of ““a fully integrated written instrument.”” *Phillips*, 415 F.3d at 1315, *quoting Markman*, 52 F.3d at 978. The claims “must be read in view of the specification, of which they are a part.” *Markman*, 52 F.3d at 979. The specification “is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.” *Phillips*, 415 F.3d at 1315, *quoting Vitronics*, 90 F.3d at 1582. The “best source for understanding a technical term is the specification from which it arose, informed, as needed, by the prosecution history.” *Phillips*, 415 F.3d at 1315, *quoting Multiform Desiccants*, 133 F.3d at 1478.

A patentee’s lexicography, either explicit or implicit, controls the meaning of the claim term. *Phillips*, 415 F.3d at 1316 (“[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor’s lexicography governs.”). Where the specification reveals an intentional disclaimer, or disavowal, of claim scope by the inventor, that intention is dispositive. *Phillips*, 415 F.3d at 1316, *citing SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1343-44 (Fed. Cir. 2001). The consistent use of a claim term throughout the specification supports the conclusion that a person of skill in the art would have understood the term as limited to that meaning. *Nystrom*, 424 F.3d at 11435 (“board” used consistently in specification to mean “wood”).

4. The Prosecution History Can Inform the Meaning of Claim Terms

Likewise, the *Phillips* Court reaffirmed that the prosecution history is part of the

intrinsic record and can be helpful in claim construction. The prosecution history can “inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be.” *Phillips*, 415 F.3d at 1317 citing *Vitronics*, 90 F.3d at 1582-83. The Court cautioned, however, that the prosecution history may be less useful than the specification because it represents an ongoing negotiation between the Patent Office and the applicant, and often lacks the clarity of the specification. *Phillips*, 415 F.3d at 1317.

5. Extrinsic Evidence Must Be Considered In the Context of Intrinsic Evidence

In addition, the *Phillips* Court reaffirmed that extrinsic evidence “consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises.” *Phillips*, 415 F.3d at 1317, quoting *Markman*, 52 F.3d at 980. Although extrinsic evidence “can shed useful light on the relevant art,” in general it is “less significant than the intrinsic record in determining ‘the legally operative meaning of claim language.’” *Phillips*, 415 F.3d at 1317 (citations omitted). When considered, extrinsic evidence must be considered in the context of the intrinsic evidence. *Id.* at 1319.

IV. Indefiniteness At The Claim Construction Stage

Title 35 of the United States Code, Section 112, requires that the specification, “. . . conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.” 35 U.S.C. § 112 ¶ 2. This requirement is known as the definiteness requirement. Courts have recognized that “the purpose of the definiteness requirement is to ensure that the claims delineate the scope of

the invention using language that adequately notifies the public of the patentee's right to exclude." *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir. 2005), quoting *Honeywell Int'l Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1338 (Fed. Cir. 2003). Thus, the determination of definiteness is necessarily "' . . . drawn from the court's performance of its duty as construer of patent claims.'" *Datamize*, 417 F.3d at 1347.

The Federal Circuit has found claims indefinite at the claim construction phase. In *Honeywell*, the patent claim at issue was for a method of producing synthetic yarn. *Honeywell*, 341 F.3d 1334. One claim term recited "thereby obtaining a drawn yarn with a terminal modulus of at least 20 g/g and a melting point elevation [MPE] of 10 C. to 14 C." *Id.* at 1335. The dispute centered on the method used for measuring the MPE, which was not recited in the claims. The specification provided a recognized definition for MPE, but three different methods of making the measurement existed - each providing different MPE numbers. *Id.* at 1336. The three measurement methods differed in how a sample of the polyethylene terephthalate yarn (PET) was prepared. Notably, the specification did not indicate which of the PET sample preparation methods was to be used. *Id.* at 1336, 1339. The district court found that the method chosen was critical in determining whether an accused yarn infringed. *Id.* at 1339. Two possible constructions were considered: (1) "'any one method'" in which an accused yarn infringed if any of the possible PET preparation methods resulted in an infringing measurement; and (2) "'all methods'" in which the accused yarn infringed only if all the methods returned a measurement within the claimed range. *Id.*

The Federal Circuit concluded that the "claims, written description, and

prosecution history do not mention the different sample preparation methods or provide sufficient clues to discern which methods are acceptable.” *Id.* The Court held the claim “insolubly ambiguous, and hence indefinite . . . [as] the claims, the written description, and the prosecution history fail to give us, as the interpreter of the claim term, any guidance as to what one of ordinary skill in the art would interpret the claim to require.” *Id.* at 1340. The Federal Circuit further noted: “Moreover, because the sample preparation method is critical to discerning whether a PET yarn has been produced by the claimed process, knowing the proper sample preparation method is necessary to practice the invention.” *Id.*

Some courts have first attempted to construe the claims before considering indefiniteness.⁶ Baxter submits some terms in the ‘191 patent claims are “insolubly ambiguous,” as was the method of measuring MPE was in the *Honeywell* case, and are, therefore, incapable of construction. In the event this Court determines it can construe all of the disputed claim terms, however, Baxter reserves all rights to argue that the asserted claims are indefinite.

V. Level Of Ordinary Skill In The Art

As the Phillips court recognized, claim terms are properly construed as viewed through the eyes of a person of ordinary skill in the art. *Phillips*, 415 F.3d at 1312-1313. In this case, a person of ordinary skill in the art would be a process chemist, biochemist or immunologist (or the equivalent) with either:

- (1) a Bachelor's or Master's degree in chemistry, biology, biochemistry,

⁶ See, e.g., *Pharmastem Therapeutics, Inc. v. Viacell Inc.*, 2003 WL 124149, *1 (Sleet, J., D. Del., Jan. 13, 2003) (Ex. A hereto); *Biovail Labs Int'l. v. Impax Labs, Inc.*, 433 F. Supp. 2d 501, 522 (E.D. Penn. 2006).

immunology, or related field, and several years of experience in one or more of the following:

- (a) the purification of blood proteins, including fractionation;
 - (b) virus removal or inactivation techniques, including solvent/detergent treatment and low pH incubation; and
 - (c) the complement system and/or ACA, including how to measure and lower ACA; or
- (2) the equivalent of (1).

VI. Proper Construction Of Disputed Claim Terms In The '191 Patent

For those claim terms that are not so indefinite that they are incapable of construction, their construction is apparent from the claim language itself, the specification and/or the prosecution history as understood by a person of ordinary skill in the art. Extrinsic evidence is generally unnecessary to construe these claim terms, but is helpful to put a few claim terms in context.

A. “Any Virus Activity”

Step (a) of Claim 1 of the '191 patent describes contacting an antibody solution with a trialkylphosphate/detergent “under conditions sufficient to substantially reduce any virus activity...” Rogaski Decl., Ex. 2, Claim 1, emphasis added. The meaning of “any virus activity” is very straightforward, as becomes clear from a review of the claims of the '191 patent. In particular, no limitation is placed upon “virus activity” in Claim 1. In contrast, Claim 21 (not asserted in this case, but still part of the specification that can inform the meaning of asserted claim terms) and Claim 23 both refer to “lipid enveloped viruses,” which is narrower than “any viruses.” The applicant clearly knew how to limit claims to “lipid enveloped viruses” where intended. Yet, despite knowing how to limit

viruses to “lipid enveloped viruses,” the applicant did not so limit Claim 1. Accordingly, “any virus activity” as used in Claim 1 is broader than “lipid enveloped viruses.”

The specification supports this construction. The “Field” portion of the Background of the Invention refers to “a virus inactivation step,” without specifying what type of viruses are inactivated. Rogaski Decl., Ex. 2, Col. 1:8-12. Similarly, the applicant describes an “inherent hazard” with antibody preparations of “transmitting virally-mediated diseases. Inactivation of viruses is an important step in producing safe and effective blood products.” Rogaski Decl., Ex. 2, Col. 1:42-45. This discussion also does not limit the types of viruses that may be present in the solution. Finally, the solvent/detergent treatment recited in Claim 1 is touted as resulting in “a product with an acceptable viral inactivation ...” Rogaski Decl., Ex. 2, Col. 2:6-10. Based on the repeated usage of “viruses” or “viral” in the specification, without qualification, there can be no question that “any virus activity” encompasses the “activity of all viruses in solution.”

B. “Under Conditions ... Resulting In An Increased Level Of Anticomplement Activity”

Claim 1 contains the requirement that the conditions under which solvent/detergent treatment is carried out result in “an increased level of anticomplement activity.” The applicant knew, when filing the application leading to the ‘191 patent, that not all conditions for solvent/detergent treatment resulted in increased levels of ACA (to an “unacceptable level”⁷). Because the particular conditions that increase ACA levels are not specified in Claim 1, this claim term is not susceptible to a sufficiently precise

⁷ See Section VI.D., below, regarding the requirement that solvent/detergent treatment increases ACA to levels unacceptable for intravenous administration.

construction and should be found indefinite.

If not found indefinite, the particular conditions that actually result in an increased ACA level to unacceptable levels should be included in the construction of this term. The intrinsic evidence provides some guidance regarding which solvent/detergent treatment conditions result in increased ACA to unacceptable levels, and which conditions do not, though the specification also repeatedly – and incorrectly (according to the named inventor’s own data) – states that solvent/detergent treatments always increase ACA. *See, e.g.*, Rogaski Decl., Ex. 2, Cols. 2:10-14 and 5:47-49. The extrinsic evidence (namely, the experiments performed by the named inventor or his team that were not disclosed to the Patent Office) demonstrates the named inventor knew that not all conditions of solvent/detergent treatment increase ACA to unacceptable levels; rather, only particular conditions cause such a result. As such, the extrinsic evidence shows the applicant’s repeated representations – that all solvent/detergent treatments (without limitation) “always” result in “increased” ACA – to be untrue. Because the extrinsic evidence here more accurately reflects the “invention,” it should be given considerable weight in construing this term. Claim 1 should be limited to the particular conditions that increase ACA. The intrinsic (and extrinsic) evidence confirms that these conditions are treatment with TNBP/ cholate at a pH of 7.0.

1. TNBP/Tween Treatment Generally Does Not Result In An Increased Level Of Anticomplement Activity

All samples but one reported in the ‘191 patent were treated with TNBP/cholate, the exception being one sample treated with TNBP/Tween. The TNBP/Tween-treated sample was reported in Table 1 as having an ACA value of 68 CH₅₀ units/mL (an “unacceptable” ACA level as discussed below) following solvent/detergent treatment at

pH 7.0. Every other sample reported in the '191 patent was treated with TNBP/cholate. The applicant's single data point for Tween is not within the "conditions ... resulting in an increased level of anticomplement activity," however, because other experiments performed by the named inventor with TNBP/Tween – which he chose not to disclose to the Patent Office – show the more common result is to have acceptable ACA levels following treatment with TNBP/Tween.

Specifically, the named inventor, Dr. Alonso's, team performed an experiment in 1993 (two years before the application leading to the '191 patent was filed, but in the same time period that the data reported in the '191 patent was obtained)

REDACTED

On another occasion, also prior to the filing of Dr. Alonso's patent application,

REDACTED

Contrary to the single Tween data point reported in the '191 patent,

REDACTED

it

becomes clear that the 68 CH₅₀ units/mL reported in the '191 patent was the exception,

rather than the rule, yet that was the only value reported for Tween. In view of the entirety of the TNBP/Tween data, this claim limitation should be construed to exclude solvent/detergent treatment with TNBP/Tween.

2. TNBP/Cholate Treatment At pH 5.8 Generally Does Not Result In An Increased Level Of Anticomplement Activity

The results reported in the '191 patent – as well as those not reported – also demonstrate that treatment with TNBP/cholate only increases ACA to unacceptable levels when the TNBP/cholate treatment occurs at pH 7.0, as opposed to pH 5.8. The following table shows data reported in the '191 patent (and one data point not reported in the '191 patent, **REDACTED**

REDACTED regarding solvent/detergent treatment with TNBP/cholate at different pHs.

ACA Results for TNBP/Cholate Treatment at pH 7.0 v. 5.8

pH	ACA after treatment with TNBP/cholate	Cite
7.0	>100 (5% solution)	'191 patent, Table 1
7.0	>100 (5% solution) >100 (5% solution) >100 (5% solution) >100 (5% solution)	'191 patent, Table 3
7.0	>100 (5% solution)	'191 patent, Table 5
REDACTED		
5.8	43 (5% solution) 31 (5% solution) 44 (5% solution) 122 (5% solution) >100 (10% solution) 49 (10% solution) 53 (10% solution)	'191 patent, Table 7

These results clearly show that treatment with TNBP/cholate at pH 7.0 always increases ACA levels to unacceptable levels (>100). In contrast, when treatment with TNBP/cholate is carried out at pH 5.8, only one in five results for a 5% solution had an increase to an unacceptable ACA level (greater than 45 CH₅₀ units/mL, as defined by the '191 patent) after TNBP/cholate treatment; and only one in three results for a 10% solution had an increase to an unacceptable ACA level (greater than 60 CH₅₀ units/mL, as defined by the '191 patent) after TNBP/cholate treatment. *See*, Rogaski Decl., Ex. 2, Col. 5:57-58 and Col. 5:61-63. Claim 1 should be construed as limited to those conditions that typically result in increased ACA levels to unacceptable levels; its construction should not be based on outlier data. Thus, only the conditions actually resulting in an increase to unacceptable ACA levels should inform the construction of the claim term “under conditions ... resulting in an increased level of anticomplement activity.” Accordingly, the proper construction of this term – “adding TNBP and cholate in an amount known to the artisan to reduce virus activity, at a pH of about 7.0 for a time known to the artisan to reduce virus activity” – becomes apparent. Any broader definition would be contrary to the usage in the specification, would ignore the data the applicant obtained but chose not to report to the Patent Office and would render the claim indefinite.

C. “Under Conditions Sufficient To Substantially Reduce Any Virus Activity And Resulting In An Increased Level Of Anticomplement Activity”

Plaintiffs proposed that this term required construction in addition to the term above. Defendants believe this term requires no different construction than that proposed for the above claim term. The only additional language is “... sufficient to substantially reduce any virus activity ...” The claim term “any virus activity” is already defined,

above. What remains of this term – “sufficient to substantially reduce” requires no construction. It means just what it says: that the TNBP/detergent treatment is “sufficient to substantially reduce” any virus activity in the solution.

D. “Increased Level Of Anticomplement Activity”

Step (a) of Claim 1 requires that TNBP/detergent treatment results in an “increased level of anticomplement activity.” The word “increased” was added in an amendment by the applicant during prosecution of the ‘191 patent (the prior modifier “given” was removed). *See* Docket No. 161, Joint Appendix (“JA”) 88. Upon first glance, it might appear that the ACA level must merely increase to some undetermined amount. However, upon further inspection of the intrinsic evidence, it becomes clear that the ACA level must increase to a level unacceptable for intravenous administration. Moreover, the increase must be from a level acceptable for intravenous administration.

1. Increase To An “Unacceptable Level”

The meaning of “increased level” in step (a) must be determined by evaluating the context of that term in view of the language in step (b) of Claim 1. Step (b) of Claim 1 requires incubation under conditions sufficient to reduce the increased ACA of step (a) “to an acceptable level suitable for intravenous administration.” Rogaski Decl., Ex. 2, Claim 1 (emphases added). Unless the ACA was at a level unacceptable for intravenous administration after step (a), there would be no need to reduce it to an acceptable level in step (b). This plain reading of Claim 1 is amply supported by both the specification and the prosecution history and requires the TNBP/detergent treatment of step (a) to increase ACA to a level unacceptable for intravenous administration.

In the specification, the applicant stated the incubation step reduces “the anticomplement activity (ACA) resulting from viral inactivation treatment of a solution

of antibodies ... to an acceptable level.” *See* Rogaski Decl., Ex. 2, Abstract. This makes clear that the incubation step is necessary to reduce ACA to acceptable levels (*i.e.*, without the incubation step, the ACA level would be unacceptable). Later, the applicant unequivocally confirmed that the solvent/detergent treatment of step (a) “results in a product with an acceptable viral inactivation but with unacceptably high levels of ACA.” Rogaski Decl., Ex. 2, Col. 2:6-10 (emphasis added). The applicant makes this unequivocal by stating, “[w]e have discovered that the incubation step [*i.e.*, step (b) of claim 1] is necessary to achieve an acceptable level of ACA low enough to allow the [immunoglobulins] to be administered by intravenous administration.” Rogaski Decl., Ex. 2, Col. 2:31-34 (emphasis added); *see also*, Rogaski Decl., Ex. 2, Col. 7:20-24 (“... [solvent/detergent treatment] yields a product which has high ACA and is unsuitable for intravenous administration.”). There can be no question that, without the incubation step of step (b), the ACA level of the alleged invention would not be low enough to administer intravenously, *i.e.*, would not be “acceptable.”

The prosecution history is in accord with this construction. For example, the applicant stated, “the conditions pH, temperature and ionic strength of step (b) must be selected to reduce the ACA to an acceptable level for IV administration.” Docket No. 161, JA 90 (emphasis added). The applicant further relied on the Figure in the ‘191 patent which purports to show ACA levels for a 5% solution at 25 CH₅₀ units/mL (which is “acceptable”) for the control, 60 CH₅₀ units/mL (which is above the “acceptable” level of 45 CH₅₀ units/mL for a 5% solution as defined in the ‘191 patent) after solvent/detergent treatment and 23 CH₅₀ units/mL (which is “acceptable”) after incubation. *Id.* In the same amendment, the applicant amended the claims arguing that

“[t]he amendments require that the incubation step (b) decreases the amount of anticomplement activity (ACA) *caused* by step (a).” *Id.* at JA 88 (emphasis added).

Lastly the applicant argued in his opening appeal brief to the Patent Board of Appeals, “[i]f there is no such increase [in anticomplement activity from step (a)], then step (b) of the invention, and *the invention itself*, is not needed.” *Id.* at JA 98 (emphasis added).

Indeed, the Decision on Appeal accepts this argument, finding, “the claimed subject matter requires that the inactivation step result in an increase in ACA levels, and a reduction in that claimed increase by the incubation step *to a point where the solution is suitable for intravenous use.*” *Id.* at JA 125 (emphasis by bold/italics added; emphasis by underlining in original). The Board also stated that treating a solution with solvent/detergent results in an increase in ACA which, even after subsequent treatment according to Tenold, purportedly does not “result in a product having acceptable ACA levels when measured immediately.” *Id.* at JA 127-128. This confirms the “increased level” after step (a) must be unacceptable.

The prosecution history further affirms that the skilled artisan would have understood step (a) of the claim to result in, “an increased level of anticomplement activity to a level unacceptable for intravenous administration.” The “invention itself, is not needed,” according to the applicant, if step (a) does not increase the anticomplement activity level. However, step (b), “the invention itself,” reduces “the increased anticomplement activity . . . to an acceptable level suitable for intravenous administration.” Because step (b) reduces anticomplement activity to an acceptable level, and is not needed absent the increase provided by step (a), the increase of step (a) must, logically, be to a level unacceptable for intravenous administration. Accordingly, it is

clear that “increased level of anticomplement activity” requires that the ACA level be increased to a level “unacceptable” for intravenous administration.

2. Increase From An Acceptable Level

The term “increased” also implies that the ACA level must be increased from some prior lower level. Because the intrinsic evidence makes clear that the increase must be to a level unacceptable for intravenous administration, it logically requires that the increase be from a level acceptable for intravenous administration. Indeed, as discussed above, the Figure in the ‘191 patent shows a comparison between a “control”⁸ (having acceptable ACA levels) and a post-solvent/detergent treated sample (having unacceptable ACA levels). Indeed, the applicant represented to the Patent Office that, “step (a) of the claimed methods results in an increase in ACA from the starting material” Docket No. 161, JA 98 (emphasis added).

The applicant’s statements to the Patent Office make clear that it believes the ACA levels prior to solvent/detergent treatment are “acceptable.” Thus, “increased level of anticomplement activity,” properly construed, means, “increased anticomplement activity from a level acceptable for intravenous administration to a level unacceptable for intravenous administration.”

E. “Increased Anticomplement Activity Of The Solution”

This claim term appears in step (b) of Claim 1. It differs from the above claim

⁸ The “control” shown in the ‘191 patent is not actually the starting material; rather, it is a sample processed in the same way as the solvent/detergent treated samples (except in some cases at a different pH value) only without a solvent/detergent treatment step. Yet, it appears the applicant considers this to be equivalent to the “starting material” and, therefore, compares the unacceptable post-solvent/detergent treatment ACA levels to the acceptable ACA level of the so-called control.

term primarily by the phrase “of the solution.” It is unclear to what “solution” this claim term refers. Is it the “solution of antibodies” of the preamble? Is it the “solution” that is contacted with a solvent/detergent treatment in step (a)? Or, is it the “solution of step a)” that results from step (a) and is then incubated in step (b)? The specification provides no guidance, confirming this claim term is indefinite.

If capable of construction, this claim term should be construed to mean “increased anticomplement activity of the solution from a level acceptable for intravenous administration to a level unacceptable for intravenous administration.”

F. “Then Incubating The Solution Of Step a)”

Claim 1 requires first treating a solution of antibodies with solvent/detergent in step (a) and “then incubating the solution of step a)” to reduce its ACA to an acceptable level. The plain language of Claim 1 itself makes abundantly clear that no steps can intervene between the solvent/detergent treatment step (step (a)) and the incubation step (step (b)). First, step (b) follows step (a), so the order of those steps is unambiguous. Second, the claim language states “and b) then incubating the solution of step a),” which requires that step (b) (incubation) occurs immediately after step (a) (solvent/detergent treatment). Finally, the language of this claim term “and b) then incubating the solution of step a)” confirms the named inventor intended that there be no steps between step (a) and step (b), *i.e.*, the solution resulting from step (a) is the solution being incubated.

There is only one “solution of step a).” It is the solution of antibodies described in step (a) that has been contacted with a trialkylphosphate and a detergent. No other treatment is identified in step (a) of Claim 1 or prior to step (b). If other steps were permitted between step (a) and step (b), the solution incubated in step (b) would no longer be the “solution of step a).” Rather, it would be a different solution that was not

only solvent/detergent treated, but also treated in some other way.

Had the applicant intended other steps to intervene between step (a) and step (b), he would have written Claim 1 differently. For example, he might have omitted “of step a)” and simply required “and b) then incubating the solution under conditions . . .”

Alternatively, he might have made express what steps could occur between step (a) and step (b), as he did when he amended the (initially) identical claim 1 in the European Patent Office (“EPO”), by adding an express step for removal of the solvent and detergent.⁹

Specifically, during prosecution of the corresponding European claims, the applicant originally submitted to the EPO the exact language of Claim 1 that was originally prosecuted in the United States. Without any urging by the EPO, the applicant amended the original Claim 1 to read as follows:

⁹ The applicant added this limitation in Europe without any prompting from the EPO, and not pursuant to any requirement under European law. *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006) (foreign prosecution not relevant for construing U.S. claims only when amendments made in foreign jurisdiction pursuant to the law of the foreign jurisdiction.) Accordingly, this amendment in Europe is relevant to the proper construction of this claim term in the United States.

Original Claim 1 in EPO:	Amended Claim 1 in EPO (additions/modifications shown in underline):
<p>1. A method of treating a solution of antibodies which may have virus activity, the method comprising</p> <p>a) contacting the solution with a trialkylphosphate and a detergent under conditions sufficient to substantially reduce any virus activity and resulting in a given level of anticomplement activity; and</p> <p>b) then incubating the solution of step a) under conditions of controlled time, pH, temperature, and ionic strength, such that the anticomplement activity of the solution is reduced to an acceptable level suitable for intravenous administration.</p>	<p>1. A method <u>for the preparation of an antibody solution having low viral activity</u>, the method comprising</p> <p>a) contacting a <u>first antibody solution</u> with a trialkylphosphate and a detergent under conditions sufficient to substantially reduce <u>viral activity present in the first antibody solution to produce a second antibody solution</u>; and</p> <p>b) <u>removing trialkylphosphate and detergent from the second antibody solution to produce a third antibody solution</u>; and</p> <p>c) incubating the <u>third antibody solution for a period of at least about ten days at a pH maintained between about 3.5 and about 5.0, a temperature within a range of about 2°C to about 50°C, and at an ionic strength of less than about 0.001 to produce the antibody solution having low viral activity and low anticomplement activity.</u></p>

Through these amendments, the applicant expressly included a step for removing the TNBP/detergent (now European step b) between the solvent/detergent treatment step (a) and the incubation step (now European step c). Rogaski Decl., Ex. 26, p. 21 and Ex. 27.

The applicant clearly knew how to claim removal of solvent and detergent from the treated antibody solution when he intended to do so; yet Claim 1 in the '191 patent was not so drafted (or amended). Because Claim 1 is specifically drafted to require the solvent/detergent treated "solution of step a)" to be "then" incubated, no intervening steps are permitted within the plain meaning of this claim (*i.e.*, removal of solvent/detergent

would occur after the incubation of step (b)). Accordingly, the proper construction of “then incubating the solution of step a)” is “incubating the solvent-detergent treated solution resulting from step a) without any additional processing steps between steps a) and b).”

G. “About 60 CH₅₀ units/mL”

Claim 2 requires that the claimed 10% solution have ACA levels less than “about 60 CH₅₀ units/mL.” As discussed above in Section II.D, there is a sometimes large variability associated with ACA measurements. The variability of ACA results depends in large part on the particular assay used to measure ACA. And, aside from the question of variability within a single ACA assay, each ACA assay can give a different result. Indeed, Bayer’s own Director of Clinical Research, Dr. Ralph Rousell, evaluated results from two internal Bayer ACA assays – one validated for a product formulated at pH 6.8 and another validated for a product formulated at pH 4.25. Bayer’s pH 4.25 product was tested with both ACA assays. The assay validated for the prior pH 6.8 product gave different ACA results than the assay validated for the pH 4.25 product. Dr. Rousell further found that the results from the two assays could not be correlated with each other (*i.e.*, a higher ACA value when tested with the pH 6.8 assay did not necessarily correspond to a higher ACA value when tested with the pH 4.25 assay). Specifically, he testified:

REDACTED

In fact, Dr. Rousell testified

REDACTED

Thus, a result of “about 60

CH₅₀ units/mL” alone is meaningless without reference to a particular assay; and a result of “about 60 CH₅₀ units/mL” with one ACA assay does not necessarily mean the same sample tested with a different ACA assay will also yield a result of about 60 CH₅₀ units/mL. As a result, this claim term is not susceptible to a sufficiently precise construction.

If the Court believes this claim term is capable of construction, at best, it must be construed in view of the particular assay used to obtain the ACA values in the ‘191 patent. Though an “assay” is briefly mentioned in the ‘191 patent at Col. 6:1-16, this description is so general as to encompass all ACA assays that involve red blood cell lysis, yet as discussed above, different assays can yield different ACA results. Thus, a description of the particular assay used to measure ACA levels in the ‘191 patent examples is required to give meaning to the term “about 60 CH₅₀ units/mL.” If capable of construction at all, this term should be construed to mean “about 60 CH₅₀ units/mL, as determined by the particular anticomplement activity assay used to obtain the anticomplement activity data reported in the ‘191 patent.”

H. “Anticomplement Activity”

Claim 1 of the ‘191 patent refers to “an increased level of anticomplement activity” and “increased anticomplement activity of the solution.” Claim 1 (emphases added). As discussed above, ACA, without reference to a particular assay, is indefinite.

To the extent the Court finds this term capable of construction, it must be

construed in view of the particular assay used to obtain the ACA values in the '191 patent. While ACA is referred to throughout the specification, a precise definition is not provided. And, as discussed above, the ACA of a solution is measured by an ACA assay that must be specifically validated for the solution, or product, being tested. The connection between ACA and the assay used to determine the ACA levels is recognized by the applicant in the specification: "one unit of ACA activity (one CH₅₀ unit) is defined as the amount of protein capable of activating 50% of the complement in an optimally titrated complement and red blood cell/hemolysin system." As each "optimally titrated complement and red blood cell/hemolysin system" is somewhat different, ACA must be defined in terms of the assay used to measure it.

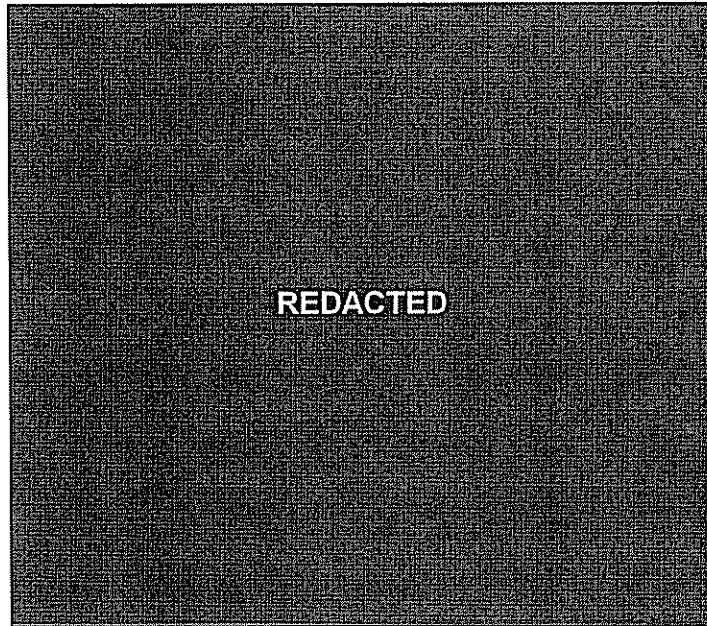
Accordingly, if capable of construction, the proper definition of "anticomplement activity" is "the amount of protein capable of activating 50% of the complement in an optimally titrated complement and red blood cell/hemolysin system, as determined by the particular anticomplement activity assay used to obtain the anticomplement activity data reported in the '191 patent."

I. "Acceptable Level Suitable For Intravenous Administration"

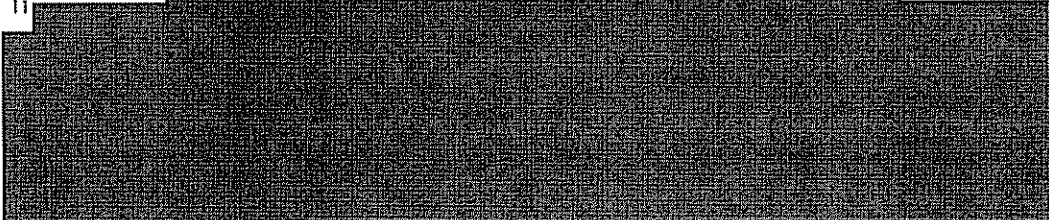
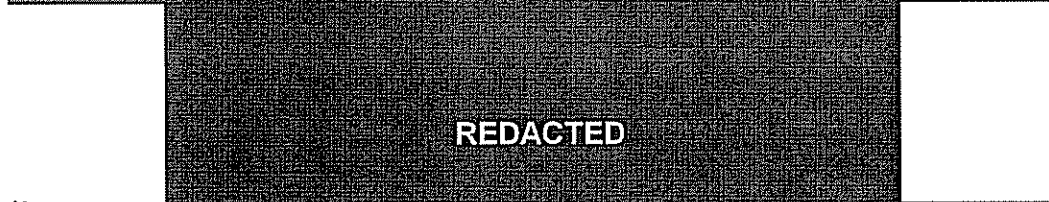
Claim 1 requires that the incubation of step (b) reduce the ACA to an "acceptable level suitable for intravenous administration." In view of the inability to compare ACA levels obtained with different ACA assays, as discussed above, this claim term is indefinite and incapable of precise construction. Indeed, the indefiniteness of this term is amply confirmed by the inability of both the named inventor and the prosecuting patent attorney to define what is "acceptable" or "unacceptable." If neither the named inventor nor the prosecuting attorney knew what "acceptable" meant at the time the patent application that resulted in the '191 patent was filed, how can one of ordinary skill in the

art know what this term means, and whether a particular ACA level is acceptable?

For example, Dr. Alonso testified in deposition:



When asked about the acceptability of a particular ACA result of 49 CH₅₀ units/mL (after incubation of a 5% solution), Dr. Alonso testified:



REDACTED

The variability of the ACA assays also impacts what is “acceptable.” One of Bayer’s patent attorneys who prosecuted, and apparently prepared, the patent application that became the ‘191 patent testified:

REDACTED

REDACTED

REDACTED

Because Claim 1 does not

specify any such variables, this term is indefinite. To give sufficient definiteness to this claim term, at least the ACA assay used must be identified, so at least one of the variables that impact the acceptability of the ACA results is known.

If capable of construction, this term must be construed in view of the specification and prosecution history. The applicant told the Patent Office that: “the acceptable level of ACA generally depends on IGIV concentration and examples (for 5 and 10% IGIV solutions) are described in the second full paragraph of page 9 [of the application].” Docket No. 161, JA 77. Page 9 of the application corresponds to Col. 5:57-61 in the ‘191 patent for a 5% solution and Col. 5:61-64 in the ‘191 patent for a 10% solution. There, the applicant represented that for a 5% solution, an “acceptable level” was “less than about 45 CH₅₀ units/mL,” and for a 10% solution, an “acceptable level” was “less than about 60 CH₅₀ units/mL.” Because ACA levels are dependent on the assay which determines them, the proper definition for this term (if capable of construction) is “a defined numerical level that depends upon the protein concentration, specifically, 60 CH₅₀ units/mL for a 10% solution and 45 CH₅₀ units/mL for a 5% solution, as determined by the particular anticomplement activity assay used to obtain the anticomplement activity data reported in the ‘191 patent.”

VII. Conclusion

Baxter’s proposed constructions of the claim terms in dispute are properly based on the claims, the specification and the prosecution history. Extrinsic evidence is generally not needed to construe the claim terms in dispute, except where the extrinsic evidence provides a more accurate interpretation of the claim terms than does the intrinsic evidence. In such limited circumstances, the extrinsic evidence should inform the meaning of the claim terms. Baxter, therefore, respectfully requests that its proposed

claim construction be adopted for those terms that are capable of construction. Baxter further requests that those terms incapable of construction be found indefinite.

POTTER ANDERSON & CORROON LLP

OF COUNSEL:

James G. Gilliland, Jr.
Susan M. Spaeth
Anne M. Rogaski
TOWNSEND AND TOWNSEND AND
CREW LLP
379 Lytton Avenue
Palo Alto, California 94301
(650) 326-2400

By: /s/ Philip A. Rovner
Philip A. Rovner (#3215)
Hercules Plaza
P.O. Box 951
Wilmington, Delaware 19899-0951
(302) 984-6000
Email: provner@potteranderson.com

*Attorneys for Defendant
Baxter International Inc. and
Defendant/Counterclaimant
Baxter Healthcare Corporation*

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**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

CERTIFICATE OF SERVICE

I, Philip A. Rovner, hereby certify that on November 3, 2006, the within document was filed with the Clerk of the Court using CM/ECF which will send notification of such filing(s) to the following; that the document was served on the following counsel as indicated; and that the document is available for viewing and downloading from CM/ECF.

BY HAND DELIVERY AND E-MAIL

Jeffrey B. Bove, Esq.
Mary W. Bourke, Esq.
Mark E. Freeman, Esq.
Jaclyn Mason, Esq.
Donna Hallowell
Connolly Bove Lodge & Hutz LLP
1007 N. Orange Street
P. O. Box 2207
Wilmington, DE 19899-2207
jbove@cblh.com, mbourke@cblh.com
mfreeman@cblh.com, jmason@cblh.com
dhallowell@cblh.com

I hereby certify that on November 3, 2006 I have sent by E-mail and Federal Express the foregoing documents to the following non-registered participants:

Bradford J. Badke, Esq.
Gabrielle Ciuffreda, Esq.
Ropes & Gray LLP
1251 Avenue of the Americas
New York, NY 10020-1105
bradford.badke@ropesgray.com
gabrielle.ciuffreda@ropesgray.com

/s/ Philip A. Rovner
Philip A. Rovner (#3215)
Potter Anderson & Corroon LLP
Hercules Plaza
P. O. Box 951
Wilmington, DE 19899
(302) 984-6000
provner@potteranderson.com